



## An Analytical Approach to the Thrombogram

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# An analytical approach to the thrombogram

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Data from thrombin generation experiments are conventionally analyzed using the so-called *thrombogram*. Commercially available instruments do this automatically but are black boxes: the exact method of analysis is hidden from the user.

In research, flexible and transparent methods of data analysis are needed. Research should not be limited by the requirements of a specific experimental setup or a specific protocol. Here we present transparent and flexible analytical methods of data analysis for thrombin generation experiments.

We show that calibration signals can be described with Michaelis-Menten kinetics of the basic enzymatic reaction and that kinetic constants and the standard calibration factor used by CAT can be extracted from the fits to raw data. We also show that thrombin generation signals can be described with a phenomenological model based on the cascade of basic enzymatic reactions that includes damping by anti-enzymes. This model also accounts for the contribution of  $\alpha_2$ -macroglobulin-thrombin complex in the raw signal and separates it from the contribution of thrombin.

We compared our method with the commercially available CAT method, using the CAT calibration factor in both methods, and found the results to be similar. However, the different interpretation of the calibration factor suggested by our model resulted in up to 1.8 fold difference between the values obtained with the two methods for ETP, peak, and velocity index parameters.

In conclusion, we have developed an analytical open-source method of data analysis in thrombin generation experiments. It is flexible, it works with an arbitrary experimental protocol, and it operates on the raw data. Therefore, its performance can easily be assessed visually, and its results are noise-robust and reliable.

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